

REMARKS

Preliminary Remarks

Claims 20, 29, 38-40, 68, 75-80, and 85-92 are amended, and new claims 93-100 are added.

Independent claims 20 and 80 are amended to be directed to a kit comprising at least one container containing substantially purified dimeric, tetravalent, CH2 domain-deleted antibodies that bind specifically to TAG-72. Independent claims 29 and 85 are similarly amended to be directed to substantially purified dimeric, tetravalent, CH2 domain-deleted antibodies that bind specifically to TAG-72. Dependent claims 38-40, 68, 75-79, and 86-92 are amended to be directed to the kit and dimeric, tetravalent antibodies of the amended independent claims. Clear support for the amendment is found in the specification. For example, page 51, lines 23-30 describes the isolation of a mixture of CH2 domain-deleted CC49 antibodies by Protein G affinity chromatography that contains approximately equal amounts (wt/wt) of monomeric (H₂L₂) and dimeric (H₄L₄) CH2 domain-deleted CC49 antibodies (*see* Figure 9). Page 52, lines 1-14, describes using HPLC size-exclusion chromatography to purify dimeric (H₄L₄) CH2 domain-deleted CC49 antibodies from contaminating monomeric (H₂L₂) antibodies to produce a preparation of substantially purified dimeric (H₄L₄) CH2 domain-deleted anti-TAG72 antibodies of the invention.

New claims 93-100 are directed to the kit and isolated dimeric, tetravalent antibodies of the amended independent claims, wherein the isolated dimeric tetravalent antibodies are substantially purified from antibodies having fewer than four antigen binding sites, and are greater than 98% purified. Support for new claims 93-100 is found in the specification, for example, on page 53, lines 1-3, which describes analysis showing that a disclosed preparation of purified dimeric, tetravalent, CH2 domain-deleted anti-TAG72 antibodies is greater than 98% purified.

Patentability Remarks**35 U.S.C. §103(a)**

Claims 20, 29, 38-40, 55, 62-63, 68, 75-81, and 84-92 are rejected under 35 U.S.C. §103(a) as being obvious in view of Gillies et al. (1990, Human Antibodies and Hybridomas, 1(1):47-54), as evidenced by the specification, in view of Kashmiri et al. (5/11/2000, WO 00/26394), Anderson et al. (U.S. Patent No. 6,348,581 B1) and Thorpe et al. (U.S. Patent No. 6,342,219 B1).

To establish a *prima facie* case of obviousness, the examiner must show that the prior art references themselves or the knowledge generally available to one of ordinary skill in the art would (1) provide some suggestion or motivation to modify or combine reference teachings to obtain the claimed invention, (2) teach or suggest all of the claim limitations, and (3) provide a reasonable expectation that the claimed invention can be made or used successfully. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). *See* M.P.E.P. § 2142.

In determining if there is obviousness in the first instance, "it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *See* M.P.E.P. § 2142.

Gillies *et al.* describes chimeric antibodies ch14.18 and B72.3 in which the CH2 domains are deleted and the CH3 domain is fused directly to the hinge region, and reported that 60 kDa and 120 kDa species migrate as a single peak during non-denaturing HPLC (*see* page 50, lower left column). Gillies *et al.* describes the 60 kDa species as "HL half-molecules" that contain one heavy chain and one light chain, and the 120kDa species as "H₂L₂ dimers" that contain two heavy chains and two light chains (*see* page 49, lower right column). However, the Gillies *et al.*


reference does not describe or even suggest the possibility of the existence of dimeric, tetravalent, CH2 domain-deleted anti-TAG72 antibodies of the claimed invention. Likewise, none of the cited secondary prior art references describe or suggest making or using the claimed dimeric, tetravalent, CH2 domain-deleted antibodies which are substantially purified. In fact, prior to the applicant's discovery and purification of dimeric, tetravalent, CH2 domain-deleted anti-bodies, it was not known that such antibody complexes existed! Therefore, the prior art would not have provided one of ordinary skill in the art at the time the invention was made with a suggestion or motivation to prepare the substantially purified dimeric, tetravalent, CH2 domain-deleted antibodies of the claimed invention. Furthermore, the teachings of the prior art would not have given one of ordinary skill in the art any reasonable expectation of success in preparing substantially purified dimeric, tetravalent, CH2 domain-deleted antibodies according to the claimed invention. In view of the foregoing, the applicants submit that claimed invention would not have been obvious to one of ordinary skill in the art in view of the cited references, and withdrawal of the rejection of claims 20, 29, 38-40, 55, 62-63, 68, 75-81, and 84-92 under 35 U.S.C. § 103(a) in view of the cited references is respectfully requested.

CONCLUSION

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If the examiner identifies any points that he feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Please charge any fees or credit any overpayments associated with the submission of this response to Deposit Account Number 03-3975.

Respectfully submitted,

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